

L Number	Hits	Search Text	DB	Time stamp
1	7	human NEAR mesencephalon	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:36
7	53	Gage NEAR Fred	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 14:52
9	12		USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:00
14	28	Ray NEAR Jasodhara	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 14:56
16	444	mesencephalon	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 14:57
17	8		USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 14:57
18	225	V-MYC	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:01
19	25046	TETRACYCLINE	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:01
20	2	mesencephalon AND V-MYC AND TETRACYCLINE	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:03
21	18	mesencephalon AND V-MYC	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:27
22	19509	FGF-2 EGF PDGF GDNF CNTF IGF-1 BDNF	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:29
23	220	mesencephalon AND (FGF-2 EGF PDGF GDNF CNTF IGF-1 BDNF)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:29
24	37	mesencephalon AND (FGF-2 EGF PDGF GDNF CNTF IGF-1 BDNF) AND TETRACYCLINE	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:29
25	115	human SAME mesencephalon	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:36
27	0	(human SAME mesencephalon) AND (FGF-2 EGF PDGF GDNF CNTF IGF-1 BDNF) AND TETRACYCLINE AND V-MYC	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:37
26	17	(human SAME mesencephalon) AND (FGF-2 EGF PDGF GDNF CNTF IGF-1 BDNF) AND TETRACYCLINE	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:55

38	29	(US-6265175-\$ or US-6294346-\$ or US-6197585-\$ or US-6020197-\$ or US-6040180-\$ or US-6045807-\$ or US-6071889-\$ or US-5980885-\$ or US-5981165-\$ or US-6013521-\$ or US-5753506-\$ or US-5766948-\$ or US-5770414-\$ or US-5750376-\$ or US-5580777-\$ or US-5851832-\$ or US-6284539-\$ or US-5411883-\$ or US-5935795-\$ or US-6093802-\$ or US-6221376-\$ or US-6294383-\$).did. or (US-20020009743-\$ or US-20020039789-\$ or US-20020006660-\$ or US-20030049234-\$ or US-20040009592-\$).did. or (WO-9949014-\$ or WO-200009669-\$).did.	USPAT; US-PGPUB; DERWENT	2004/01/28 15:54
39	4	(human SAME mesencephalon) AND (FGF-2 EGF PDGF GDNF CNTF IGF-1 BDNF) AND TETRACYCLINE AND ((US-6265175-\$ or US-6294346-\$ or US-6197585-\$ or US-6020197-\$ or US-6040180-\$ or US-6045807-\$ or US-6071889-\$ or US-5980885-\$ or US-5981165-\$ or US-6013521-\$ or US-5753506-\$ or US-5766948-\$ or US-5770414-\$ or US-5750376-\$ or US-5580777-\$ or US-5851832-\$ or US-6284539-\$ or US-5411883-\$ or US-5935795-\$ or US-6093802-\$ or US-6221376-\$ or US-6294383-\$).did. or (US-20020009743-\$ or US-20020039789-\$ or US-20020006660-\$ or US-20030049234-\$ or US-20040009592-\$).did. or (WO-9949014-\$ or WO-200009669-\$).did.)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/28 15:55

> d his

(FILE 'HOME' ENTERED AT 16:52:49 ON 28 JAN 2004)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED  
AT 16:52:57 ON 28 JAN 2004

L1 5173 S MESENCEPHALON (L) NEUR?  
L2 36018 S IMMORTAL?  
L3 35 S L1 (L) L2  
L4 16 DUP REM L3 (19 DUPLICATES REMOVED)  
L5 16 SORT L4 PY  
L6 2865368 S NEUR? OR NERV?  
L7 4018 S L6 AND L2  
L8 3407 S L6 (L) L2  
L9 692 S L8 AND (STEM OR PROGEN? OR MULTIPOTEN? OR PLURI?)  
L10 41 S L9 AND TETRA?  
L11 17 DUP REM L10 (24 DUPLICATES REMOVED)  
L12 17 SORT L11 PY  
L13 1 S L10 AND C-MYC  
L14 22 S L10 AND V\ -MYC  
L15 22 S L10 AND V-MYC  
L16 22 S L15 AND TETRACYCL?  
L17 22 S L15 AND TETRACYCLINE  
L18 22 FOCUS L17 1-  
L19 22 SORT L18 PY  
L20 7 DUP REM L19 (15 DUPLICATES REMOVED)  
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E GAGE F.H./AU  
L21 279 S E5  
E SAH DINAH?/AU  
L22 25 S E1  
L23 3 S L21 AND L1  
L24 0 S L22 AND L1  
L25 223 S L21 AND L6  
L26 6 S L21 AND L9  
L27 5 S L22 AND L9

=> d an ti so au ab pi l27 1

L27 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:672982 CAPLUS

DN 131:269274

TI PNS cell lines and methods of use therefor

SO PCT Int. Appl., 84 pp.

CODEN: PIXXD2

IN **Sah, Dinah W. Y.**; Raymon, Heather K.

AB Conditionally-immortalized PNS progenitor cell lines  
are provided. Such cell lines, which may be clonal, may be used to  
generate **neurons**. The cell lines and/or differentiated cells  
may be used for the development of therapeutic agents to prevent and treat  
a variety of PNS-related diseases. The cell lines and/or differentiated  
cells may also be used in assays and for the general study of PNS cell  
development, death and abnormalities.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 9953028	A1	19991021	WO 1999-US8167	19990414
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2325603	AA	19991021	CA 1999-2325603	19990414
	AU 9936429	A1	19991101	AU 1999-36429	19990414
	EP 1071750	A1	20010131	EP 1999-918545	19990414
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,			

L26 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1998:176007 CAPLUS  
 DN 128:229000  
 TI Development of human CNS cell lines and use to study CNS cell development, death, and abnormalities  
 SO PCT Int. Appl., 76 pp.  
 CODEN: PIXXD2  
 IN Sah, Dinah W. Y.; Gage, Fred H.; Ray, Jasodhara  
 AB Conditionally-immortalized human CNS progenitor cell lines are provided. Such cell lines, which may be clonal, may be used to generate neurons and/or astrocytes. Such cell lines and/or differentiated cells may be used for the development of therapeutic agents to prevent and treat a variety of CNS-related diseases. The cell lines are produced by transfecting CNS progenitor cells with oncogenes and growing the cells on polyornithine/laminin, polylysine/laminin, or fibronectin-treated surfaces in culture medium supplemented with proliferation-enhancing factors. Suitable oncogenes include v-myc, N-myc, c-myc, p53, SV40 large T antigen, polyoma large T antigen, Ela adenovirus, and the human papillomavirus E7 protein gene. Such cell lines and/or differentiated cells may also be used in assays and for the general study of CNS cell development, death and abnormalities. Examples of abnormalities include Alzheimer's disease, stroke, traumatic head injuries, and amyotrophic lateral sclerosis.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9810058	A1	19980312	WO 1997-US15442	19970902
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9743315	A1	19980326	AU 1997-43315	19970902
AU 727113	B2	20001130		
EP 925357	A1	19990630	EP 1997-941398	19970902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001500727	T2	20010123	JP 1998-512817	19970902

L26 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1997:568304 CAPLUS  
 DN 127:201026  
 TI Regulatable retroviral vector containing v-myc oncogene for immortalization of adult neuronal progenitor cells  
 SO PCT Int. Appl., 42 pp.  
 CODEN: PIXXD2  
 IN Gage, Fred H.; Ray, Jasodhara; Hoshimaru, Minoru  
 AB A novel regulatable retroviral vector in which the v-myc oncogene is driven by a tetracycline-controlled transactivator and a human cytomegalovirus minimal promoter fused to tet operator sequence useful for immortalization of adult neuronal progenitor cells is provided. Producer cell lines which produce high titers of the recombinant retrovirus are also provided. This general method is exemplified by the retroviral vector LINXv-myc. HC2S2 cells from adult rat hippocampus were infected with the retroviral vectors. HC2S2 cells, derived from an immortalized neuronal progenitor cell, were differentiated into neurons after suppression of the v-myc oncogene.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9730168	A1	19970821	WO 1997-US2013	19970211
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5770414	A	19980623	US 1996-602203	19960220
CA 2242381	AA	19970821	CA 1997-2242381	19970211
AU 9722642	A1	19970902	AU 1997-22642	19970211
AU 721727	B2	20000713		
EP 892851	A1	19990127	EP 1997-906896	19970211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000504584	T2	20000418	JP 1997-529408	19970211

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L1 5173 S MESENCEPHALON (L) NEUR?  
L2 36018 S IMMORTAL?  
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L5 16 SORT L4 PY  
L6 2865368 S NEUR? OR NERV?  
L7 4018 S L6 AND L2  
L8 3407 S L6 (L) L2  
L9 692 S L8 AND (STEM OR PROGEN? OR MULTIPOTEN? OR PLURI?)  
L10 41 S L9 AND TETRA?  
L11 17 DUP REM L10 (24 DUPLICATES REMOVED)  
L12 17 SORT L11 PY  
L13 1 S L10 AND C-MYC  
L14 22 S L10 AND V\ -MYC  
L15 22 S L10 AND V-MYC  
L16 22 S L15 AND TETRACYCL?  
L17 22 S L15 AND TETRACYCLINE  
L18 22 FOCUS L17 1-  
L19 22 SORT L18 PY  
L20 7 DUP REM L19 (15 DUPLICATES REMOVED)  
E GAGE FRED?/AU  
E GAGE F.H./AU  
L21 279 S E5  
E SAH DINAH?/AU  
L22 25 S E1  
L23 3 S L21 AND L1  
L24 0 S L22 AND L1  
L25 223 S L21 AND L6  
L26 6 S L21 AND L9  
L27 5 S L22 AND L9

=> d an ti so au ab pi l27 1 3 4 5

L27 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1999:672982 CAPLUS  
DN 131:269274  
TI PNS cell lines and methods of use therefor  
SO PCT Int. Appl., 84 pp.  
CODEN: PIXXD2

IN Sah, Dinah W. Y.; Raymon, Heather K.

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a variety of PNS-related diseases. The cell lines and/or differentiated  
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 9953028	A1	19991021	WO 1999-US8167	19990414
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2325603	AA	19991021	CA 1999-2325603	19990414
	AU 9936429	A1	19991101	AU 1999-36429	19990414
	EP 1071750	A1	20010131	EP 1999-918545	19990414
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,			

IE, FI  
 BR 9909624 A 20010911 BR 1999-9624 19990414  
 JP 2002511248 T2 20020416 JP 2000-543576 19990414

L27 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1998:176007 CAPLUS  
 DN 128:229000  
 TI Development of human CNS cell lines and use to study CNS cell development, death, and abnormalities  
 SO PCT Int. Appl., 76 pp.  
 CODEN: PIXXD2

IN **Sah, Dinah W. Y.**; Gage, Fred H.; Ray, Jasodhara  
 AB Conditionally-**immortalized** human CNS **progenitor** cell lines are provided. Such cell lines, which may be clonal, may be used to generate **neurons** and/or astrocytes. Such cell lines and/or differentiated cells may be used for the development of therapeutic agents to prevent and treat a variety of CNS-related diseases. The cell lines are produced by transfecting CNS **progenitor** cells with oncogenes and growing the cells on polyornithine/laminin, polylysine/laminin, or fibronectin-treated surfaces in culture medium supplemented with proliferation-enhancing factors. Suitable oncogenes include v-myc, N-myc, c-myc, p53, SV40 large T antigen, polyoma large T antigen, Ela adenovirus, and the human papillomavirus E7 protein gene. Such cell lines and/or differentiated cells may also be used in assays and for the general study of CNS cell development, death and abnormalities. Examples of abnormalities include Alzheimer's disease, stroke, traumatic head injuries, and amyotrophic lateral sclerosis.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9810058	A1	19980312	WO 1997-US15442	19970902
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9743315	A1	19980326	AU 1997-43315	19970902
AU 727113	B2	20001130		
EP 925357	A1	19990630	EP 1997-941398	19970902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001500727	T2	20010123	JP 1998-512817	19970902

L27 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1997:371172 CAPLUS  
 DN 127:93276  
 TI Bipotent **progenitor** cell lines from the human CNS  
 SO Nature Biotechnology (1997), 15(6), 574-580  
 CODEN: NABIF9; ISSN: 1087-0156  
 AU **Sah, Dinah W. Y.**; Ray, Jasodhara; Gage, Fred H.  
 AB Human central **nervous** system (CNS) cell lines would substantially facilitate drug discovery and basic research by providing a readily renewable source of human **neurons**. We isolated clonal human CNS cell lines that had been **immortalized** with a tetracycline (Tc)-responsive v-myc oncogene; addn. of Tc to the growth medium suppressed the oncoprotein rapidly and virtually completely, allowing differentiation to proceed. Two classes of bipotent precursor cells were **immortalized**: the first class had a default differentiation pathway of **neurons** only, and the second class had a default differentiation pathway of **neurons** and astrocytes. We found that after exposure to different external signals in vitro, the environment is capable of redirecting the fate of a particular cell, even in the case of the bipotent precursor cell whose default differentiation pathway was **neurons** only. These data suggest that extrinsic cues can prevail over intrinsic determinants in directing cell fate in the human CNS.

L27 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 1996:123431 CAPLUS  
 DN 124:227790  
 TI Differentiation of the **immortalized** adult **neuronal progenitor** cell line HC2S2 into **neurons** by regulatable suppression of the v-myc oncogene

SO Proceedings of the National Academy of Sciences of the United States of America (1996), 93(4), 1518-23  
CODEN: PNASA6; ISSN: 0027-8424

AU Hoshimaru, Minoru; Ray, Jasodhara; **Sah, Dinah W. Y.**; Gage, Fred H.

AB A regulatable retroviral vector in which the v-myc oncogene is driven by a tetracycline-controlled transactivator and a human cytomegalovirus minimal promoter fused to a tet operator sequence was used for conditional **immortalization** of adult rat **neuronal progenitor** cells. A single clone, HC2S2, was isolated and characterized. Two days after the addn. of tetracycline, the HC2S2 cells stopped proliferating, began to extend **neurites**, and expressed the **neuronal** markers tau, NeuN, **neurofilament** 200 kDa, and glutamic acid decarboxylase in accordance with the reduced prodn. of the v-myc oncoprotein. Differentiated HC2S2 cells expressed large sodium and calcium currents and could fire regenerative action potentials. These results suggest that the suppression of the v-myc oncogene may be sufficient to make proliferating cells exit from cell cycles and induce terminal differentiation. The HC2S2 cells will be valuable for studying the differentiation process of **neurons**.

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L26 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1999:20170 CAPLUS  
DN 130:245944  
TI The use of neural **progenitor** cells for therapy in the CNS disorders

SO CNS Regeneration (1999), 183-201. Editor(s): Tuszynski, Mark H.; Kordower, Jeffrey H. Publisher: Academic, San Diego, Calif.  
CODEN: 67CYA3

AU Ray, Jasodhara; Palmer, Theo D.; Shihabuddin, Lamya S.; **Gage, Fred H.**

AB A review with 84 refs. In recent years a significant no. of **neurol.** diseases have been defined at the mol. level. Somatic gene therapy using genetically modified non-**neuronal** cells expressing therapeutic factors have been successfully used in animal models of **neurodegenerative** diseases. Ability to grow central **nervous** system (CNS)-derived **neural progenitor** cells has proven to be extremely useful to study a diverse phenomenon including the fate choice, differentiation, and synaptic maturation of cells. **Immortal** or perpetual cultures of **neural progenitor** cells implanted into the rodent brain survive, migrate, and integrate in the host cytoarchitecture. These cells can be genetically modified to express therapeutic gene products. The ability of the implanted cells to integrate in the host brain and express transgene products in situ offer potential approaches for gene therapy in certain CNS diseases. The utility of this approach has already been explored in animal models of **neurodegenerative** diseases. This chapter reviews the recent advances made in understanding the nature and potentiality of **neural progenitor** cells in vitro and in vivo as well as their possible use for cell replacement and gene therapy.

L26 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1998:176007 CAPLUS  
DN 128:229000  
TI Development of human CNS cell lines and use to study CNS cell development, death, and abnormalities

SO PCT Int. Appl., 76 pp.  
CODEN: PIXXD2

IN **Sah, Dinah W. Y.**; **Gage, Fred H.**; Ray, Jasodhara

AB Conditionally-**immortalized** human CNS **progenitor** cell lines are provided. Such cell lines, which may be clonal, may be used to generate **neurons** and/or astrocytes. Such cell lines and/or differentiated cells may be used for the development of therapeutic agents to prevent and treat a variety of CNS-related diseases. The cell lines are produced by transfecting CNS **progenitor** cells with oncogenes

and growing the cells on polyornithine/laminin, polylysine/laminin, or fibronectin-treated surfaces in culture medium supplemented with proliferation-enhancing factors. Suitable oncogenes include v-myc, N-myc, c-myc, p53, SV40 large T antigen, polyoma large T antigen, E1a adenovirus, and the human papillomavirus E7 protein gene. Such cell lines and/or differentiated cells may also be used in assays and for the general study of CNS cell development, death and abnormalities. Examples of abnormalities include Alzheimer's disease, stroke, traumatic head injuries, and amyotrophic lateral sclerosis.

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W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9743315	A1	19980326	AU 1997-43315	19970902
AU 727113	B2	20001130		
EP 925357	A1	19990630	EP 1997-941398	19970902
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001500727	T2	20010123	JP 1998-512817	19970902

L26 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:568304 CAPLUS

DN 127:201026

TI Regulatable retroviral vector containing v-myc oncogene for **immortalization** of adult **neuronal progenitor** cells

SO PCT Int. Appl., 42 pp.

CODEN: PIXXD2

IN Gage, Fred H.; Ray, Jasodhara; Hoshimaru, Minoru

AB A novel regulatable retroviral vector in which the v-myc oncogene is driven by a tetracycline-controlled transactivator and a human cytomegalovirus minimal promoter fused to tet operator sequence useful for **immortalization** of adult **neuronal progenitor** cells is provided. Producer cell lines which produce high titers of the recombinant retrovirus are also provided. This general method is exemplified by the retroviral vector LINXv-myc. HC2S2 cells from adult rat hippocampus were infected with the retroviral vectors. HC2S2 cells, derived from an **immortalized neuronal progenitor** cell, were differentiated into **neurons** after suppression of the v-myc oncogene.

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WO 9730168	A1	19970821	WO 1997-US2013	19970211
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5770414	A	19980623	US 1996-602203	19960220
CA 2242381	AA	19970821	CA 1997-2242381	19970211
AU 9722642	A1	19970902	AU 1997-22642	19970211
AU 721727	B2	20000713		
EP 892851	A1	19990127	EP 1997-906896	19970211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000504584	T2	20000418	JP 1997-529408	19970211

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FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED  
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L1 5173 S MESENCEPHALON (L) NEUR?  
L2 36018 S IMMORTAL?  
L3 35 S L1 (L) L2  
L4 16 DUP REM L3 (19 DUPLICATES REMOVED)  
L5 16 SORT L4 PY  
L6 2865368 S NEUR? OR NERV?  
L7 4018 S L6 AND L2  
L8 3407 S L6 (L) L2  
L9 692 S L8 AND (STEM OR PROGEN? OR MULTIPOTEN? OR PLURI?)  
L10 41 S L9 AND TETRA?  
L11 17 DUP REM L10 (24 DUPLICATES REMOVED)  
L12 17 SORT L11 PY  
L13 1 S L10 AND C-MYC  
L14 22 S L10 AND V\ -MYC  
L15 22 S L10 AND V-MYC  
L16 22 S L15 AND TETRACYCL?  
L17 22 S L15 AND TETRACYCLINE  
L18 22 FOCUS L17 1-  
L19 22 SORT L18 PY  
L20 7 DUP REM L19 (15 DUPLICATES REMOVED)

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L20 ANSWER 7 OF 7 MEDLINE on STN DUPLICATE 6  
AN 96202311 MEDLINE  
TI Differentiation of the **immortalized** adult **neuronal progenitor** cell line HC2S2 into **neurons** by regulatable suppression of the **v-myc** oncogene.  
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1996 Feb 20) 93 (4) 1518-23.  
Journal code: 7505876. ISSN: 0027-8424.  
AU Hoshimaru M; Ray J; Sah D W; Gage F H  
AB A regulatable retroviral vector in which the **v-myc** oncogene is driven by a **tetracycline**-controlled transactivator and a human cytomegalovirus minimal promoter fused to a tet operator sequence was used for conditional **immortalization** of adult rat **neuronal progenitor** cells. A single clone, HC2S2, was isolated and characterized. Two days after the addition of **tetracycline**, the HC2S2 cells stopped proliferating, began to extend **neurites**, and expressed the **neuronal** markers tau, NeuN, **neurofilament** 200 kDa, and glutamic acid decarboxylase in accordance with the reduced production of the **v-myc** oncoprotein. Differentiated HC2S2 cells expressed large sodium and calcium currents and could fire regenerative action potentials. These results suggest that the suppression of the **v-myc** oncogene may be sufficient to make proliferating cells exit from cell cycles and induce terminal differentiation. The HC2S2 cells will be valuable for studying the differentiation process of **neurons**.

L20 ANSWER 6 OF 7 MEDLINE on STN DUPLICATE 5  
AN 97325529 MEDLINE  
TI Bipotent **progenitor** cell lines from the human CNS.  
SO NATURE BIOTECHNOLOGY, (1997 Jun) 15 (6) 574-80.  
Journal code: 9604648. ISSN: 1087-0156.  
AU Sah D W; Ray J; Gage F H  
AB Human central **nervous** system (CNS) cell lines would substantially facilitate drug discovery and basic research by providing a readily renewable source of human **neurons**. We isolated clonal human CNS cell lines that had been **immortalized** with a **tetracycline** (Tc)-responsive **v-myc** oncogene; addition of Tc to the growth medium suppressed the oncoprotein rapidly and virtually completely, allowing differentiation to proceed. Two classes of bipotent precursor cells were **immortalized**: the first class had

a default differentiation pathway of **neurons** only, and the second class had a default differentiation pathway of **neurons** and astrocytes. We found that after exposure to different external signals in vitro, the environment is capable of redirecting the fate of a particular cell, even in the case of the bipotent precursor cell whose default differentiation pathway was **neurons** only. These data suggest that extrinsic cues can prevail over intrinsic determinants in directing cell fate in the human CNS.

L20 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:568304 CAPLUS

DN 127:201026

TI Regulatable retroviral vector containing **v-myc** oncogene for **immortalization** of adult **neuronal progenitor** cells

SO PCT Int. Appl., 42 pp.

CODEN: PIXXD2

IN Gage, Fred H.; Ray, Jasodhara; Hoshimaru, Minoru

AB A novel regulatable retroviral vector in which the **v-myc** oncogene is driven by a **tetracycline**-controlled transactivator and a human cytomegalovirus minimal promoter fused to tet operator sequence useful for **immortalization** of adult **neuronal progenitor** cells is provided. Producer cell lines which produce high titers of the recombinant retrovirus are also provided. This general method is exemplified by the retroviral vector LINXv-myc. HC2S2 cells from adult rat hippocampus were infected with the retroviral vectors. HC2S2 cells, derived from an **immortalized neuronal progenitor** cell, were differentiated into **neurons** after suppression of the **v-myc** oncogene.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9730168	A1	19970821	WO 1997-US2013	19970211

W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5770414	A	19980623	US 1996-602203	19960220
CA 2242381	AA	19970821	CA 1997-2242381	19970211
AU 9722642	A1	19970902	AU 1997-22642	19970211
AU 721727	B2	20000713		
EP 892851	A1	19990127	EP 1997-906896	19970211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000504584	T2	20000418	JP 1997-529408	19970211

L20 ANSWER 1 OF 7 MEDLINE on STN DUPLICATE 1

AN 2000145994 MEDLINE

TI Motoneuron differentiation of immortalized human spinal cord cell lines.

SO JOURNAL OF NEUROSCIENCE RESEARCH, (2000 Feb 1) 59 (3) 342-52.

Journal code: 7600111. ISSN: 0360-4012.

AU Li R; Thode S; Zhou J; Richard N; Pardinas J; Rao M S; Sah D W

AB Human motoneuron cell lines will be valuable tools for spinal cord research and drug discovery. To create such cell lines, we **immortalized NCAM(+)/neurofilament(+)** precursors from human embryonic spinal cord with a **tetracycline** repressible **v-myc** oncogene. Clonal NCAM(+)/**neurofilament** (+) cell lines differentiated exclusively into **neurons** within 1 week. These **neurons** displayed extensive processes, exhibited immunoreactivity for mature **neuron**-specific markers such as tau and synaptophysin, and fired action potentials upon current injection. Moreover, a clonal precursor cell line gave rise to multiple types of spinal cord **neurons**, including ChAT(+)/Lhx3(+)/Lhx4(+) motoneurons and GABA(+) interneurons. These **neuronal** restricted precursor cell lines will expedite the elucidation of molecular mechanisms that regulate the differentiation, maturation and survival of specific subsets of spinal cord **neurons**, and the identification and validation of novel drug targets for motoneuron diseases and spinal cord injury.

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L20 ANSWER 3 OF 7 MEDLINE on STN

DUPLICATE 3

AN 1998331982 MEDLINE  
 TI Induction of the N-methyl-D-aspartate receptor subunit 1 in the **immortalized neuronal progenitor** cell line HC2S2 during differentiation into **neurons**.  
 SO JOURNAL OF NEUROSCIENCE RESEARCH, (1998 Jun 15) 52 (6) 699-708. Journal code: 7600111. ISSN: 0360-4012.  
 AU Asahi M; Hoshimaru M; Hojo M; Matsuura N; Kikuchi H; Hashimoto N  
 AB Conditionally **immortalized neuronal progenitor** cell line HC2S2 differentiates into mature **neurons** after suppression of the **v-myc** expression with **tetracycline**. Reverse transcription-polymerase chain reaction analyses were used to measure expression levels of N-methyl-D-aspartate receptor subunit 1 (NMDAR1) mRNAs encoding splice variants (NMDAR1a, -exon 5; NMDAR1b, +exon 5) in HC2S2 cells during the differentiation. Differential induction of NMDAR1a and NMDAR1b mRNAs was observed during the differentiation. Very low expression of NMDAR1 was observed in undifferentiated HC2S2 cells. NMDAR1a mRNA was induced coincidentally with the emergence of **neurites**, whereas NMDAR1b mRNA was induced at the time of network formation. Immunohistochemistry also demonstrated induction of NMDAR1 immunoreactivity in differentiated HC2S2 cells. In addition, expression of NMDAR2 mRNA and immunoreactivity was observed in undifferentiated and differentiated HC2S2 cells, suggesting that functional NMDA receptors are present in differentiated HC2S2 cells. While exposure to NMDA resulted in almost no cell death in undifferentiated HC2S2 cells, NMDA induced cell death in differentiated HC2S2 cells in a dose-dependent fashion. These findings suggest that the expression of NMDAR1 mRNA may be regulated by myc or its counterpart during **neuronal** terminal differentiation and that the splicing choice between NMDAR1a and NMDAR1b may vary according to the formation of **neuronal** network.

L20 ANSWER 2 OF 7 MEDLINE on STN DUPLICATE 2  
 AN 1999307333 MEDLINE  
 TI **Immortalized** human dorsal root ganglion cells differentiate into **neurons** with nociceptive properties.  
 SO JOURNAL OF NEUROSCIENCE, (1999 Jul 1) 19 (13) 5420-8. Journal code: 8102140. ISSN: 0270-6474.  
 AU Raymon H K; Thode S; Zhou J; Friedman G C; Pardinas J R; Barrere C; Johnson R M; Sah D W  
 AB A renewable source of human sensory **neurons** would greatly facilitate basic research and drug development. We had established previously conditionally **immortalized** human CNS cell lines that can differentiate into functional **neurons** (). We report here the development of an **immortalized** human dorsal root ganglion (DRG) clonal cell line, HD10.6, with a **tetracycline**-regulatable **v-myc** oncogene. In the proliferative condition, HD10.6 cells have a doubling time of 1.2 d and exhibit a **neuronal** precursor morphology. After differentiation of clone HD10.6 for 7 d in the presence of **tetracycline**, **v-myc** expression was suppressed, and >50% of the cells exhibited typical **neuronal** morphology, stained positively for **neuronal** cytoskeletal markers, and fired action potentials in response to current injection. Furthermore, this cell line was fate-restricted to a **neuronal** phenotype; even in culture conditions that promote Schwann cell or smooth muscle differentiation of **neural crest stem** cells, HD10.6 differentiated exclusively into **neurons**. Moreover, differentiated HD10.6 cells expressed sensory **neuron**-associated transcription factors and exhibited capsaicin sensitivity. Taken together, these data indicate that we have established an **immortalized** human DRG cell line that can differentiate into sensory **neurons** with nociceptive properties. The cell line HD10.6 represents the first example of a human sensory **neuronal** line and will be valuable for basic research, as well as for the discovery of novel drug targets and clinical candidates.

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L5 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:133811 CAPLUS  
DN 132:177726  
TI Human mesencephalon cell lines and methods of use therefor  
SO PCT Int. Appl., 28 pp.  
CODEN: PIXXD2  
IN Sah, Dinah W.; Raymon, Heather K.  
AB Conditionally-immortalized human mesencephalon cell lines are provided. Such cell lines, which may be clonal, may be used to generate **neurons**, including dopaminergic **neurons**. The cell lines and/or differentiated cells may be used for the development of therapeutic agents to prevent and treat a variety of **neuro**l. diseases such as Parkinson's disease. The cell lines and/or differentiated cells may also be used in assays and for the general study of **mesencephalon** cell development and differentiation.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000009669	A1	20000224	WO 1999-US18403	19990812
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2340060	AA	20000224	CA 1999-2340060	19990812
AU 9954825	A1	20000306	AU 1999-54825	19990812
EP 1105464	A1	20010613	EP 1999-941107	19990812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002522070	T2	20020723	JP 2000-565106	19990812

L5 ANSWER 2 OF 16 MEDLINE on STN  
AN 96429942 MEDLINE  
TI Evidence for a novel neurotrophic factor for dopaminergic neurons secreted from mesencephalic glial cell lines.  
SO JOURNAL OF NEUROSCIENCE RESEARCH, (1996 Mar 1) 43 (5) 576-86.  
Journal code: 7600111. ISSN: 0360-4012.  
AU Engele J; Rieck H; Choi-Lundberg D; Bohn M C  
AB Our previous studies have shown that primary mesencephalic glia secrete factors that promote dopaminergic cell survival and differentiation in vitro. To obtain enough starting material to identify the **neurotrophic** activity, embryonic day (E)14.5 rat mesencephalic glia were stimulated with acidic fibroblast growth factor to increase number of cells. These cells were replated in the absence of **neurons** and **immortalized** by transfection with the SV 40 large T-antigen. Clonal cell lines were established and characterized for immunoreactivity (IR) to various glial and non-glial markers. Media conditioned by these cell lines were tested for survival-promoting effects on dopaminergic **neurons** in serum-free cultures of the dissociated E14.5 rat **mesencephalon**. All cell lines expressed IR for the astrocytic marker, GFAP, the oligodendroglial marker, CNP, and for A2B5, a marker for O-2A progenitor cells, but were negative for the **neuronal** marker, microtubule associated protein-2, and the fibroblast marker, fibronectin. Moreover, treatment of serum-free cultures of the dissociated E14.5 **mesencephalon** with glial cell line-CM conditioned medium (CM) delayed dopaminergic cell death in a dose-dependent manner, resulting in a maximal twofold to sixfold increase in the number of surviving tyrosine hydroxylase-IR **neurons** at various days in vitro. This increase in dopaminergic cell survival was not mimicked by GDNF, BDNF or NT-3 within the initial 3 days of cultivation. Moreover, initial biochemical characterization demonstrated that the **neurotrophic** activity is restricted to the high MW fraction of >50 kD of glial cell line-CM. Since the apparent MW of this factor exceeds the size of most known growth factors, it may represent a novel dopaminergic **neurotrophic** factor.

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